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10/607,050	06/27/2003	Takashi Yamamura	NITT.0144	4137

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EXAMINER	
MILLER, MARINA I	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/607,050	TAKASHI YAMAMURA	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *4-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/27/03;1/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I (claims 1-3 directed to a method of evaluation of an interferon β treatment) in the reply filed on 2/24/2006 is acknowledged. Applicants also elected the following species with traverse:

Species A: IFIT4 gene; Species B: IRF7 gene; Species C: SCYA2 gene; Species D: OL18 gene; Species E: TGFB1 gene.

The traversal is on the ground(s) that the subject matter of claims 1-6 is sufficiently related and a search and examination of the entire application would not place a serious burden on the examiner. Applicants argue that an array of Invention II is specific for Invention I (method of evaluating interferon treatment). This is not found persuasive because the inventions of Groups I-II are distinct. Specifically, Invention I is directed to a method of evaluation of an interferon β treatment. Invention II is directed to an array of probes corresponding to a set of genes deposited on a substrate. An intended use of the array (i.e., for evaluating an interferon treatment) does not make the array specific for the method of Invention I because an array of probes may be used in variety of different methods. With regard of the species election requirement, every species in Species groups A-E has different structure and function, and data generated for each gene is expected to be different and independent for data for any other gene. The examiner must search non-patent literature and foreign patents as well as U.S. patents and publications. In addition, the search required for each group is not coextensive with that required for any other group, therefore the examiner maintains that a search for more than one group and species would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-6 are pending.

Claims 4-6 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim.

An action on merits of claims 1-3, as they read on the elected species, follows.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Applicant cannot rely upon the foreign priority papers to overcome the rejections stated below because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "referring to a database." It is not clear what steps are actually intended and whether "referring" is intended to mean using, generating, linking, *etc.* or, as defined by

Merriam-Webster Dictionary: citing, supplying with a reference, or putting in form adapted to easy reference. As the intended limitation is not clear, claims 1-3 are indefinite.

Claim 1 recites "evaluating the efficacy ... based on ... gene expression levels and the correlation data." It is not clear what limitation is intended because it is not clear what standard, algorithm, strategy, and/or criteria is to be applied in order to "evaluate" data. As the intended limitation is not clear, claims 1-3 are indefinite.

Claim 1 recites "probes corresponding to at least one interferon induced protein gene, at least one interferon regulation factor gene, and at least one chemokine gene." It is not clear whether a probe "corresponds" to all three types of recited protein genes (*i.e.*, a universal probe which hybridizes to all three interferon-affected protein genes); different probes "correspond" to only one type of a recited interferon-affected protein gene; or one probe "corresponds" to multiple interferon induced protein genes, one probe corresponds to multiple interferon regulation factor genes, and one probe "corresponds" to multiple chemokine genes. Also, it is not clear what parameters are to be assessed and to what degree, in order to determine a "correspondence." As the intended limitation is not clear, claims 1-3 are indefinite.

Claim 1 recites in the preamble "an evaluation method of an interferon β treatment." The last method step also recited "evaluating the efficacy of the interferon β treatment." Other steps of the method do not recite treating a subject with an interferon β, and only recite hybridizing a sample with probes corresponding to interferon-affected protein genes. Therefore, the relationships between the preamble and the last step and other steps of the method is not clear. As the intended limitation is not clear, claims 1-3 are indefinite.

Claim 1 recites the limitation "detecting fluorescence to thereby determine the expression." It is not clear whether "to thereby determine" is intended to be an active, positive method step, *i.e.*, whether the expression levels are actually determined. As the intended limitation is not clear, claims 1-3 are indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sharp US 2003/0104393, in view of Veer, *Genomics*, 54:267-277 (1998), and further in view of Satoh, *Neurology*, 57:681-685 (2001).

Sharp discloses a method of assessing an effect in an organism caused by different factors based on gene expression profile (abstract). Sharp discloses a labeling with a fluorescent dye an mRNA sample derived from blood cells, mixing and hybridizing the sample with probes corresponding to test genes, expression of which is induced by a factor, and detecting fluorescence indicative of a level of the gene expression [0040], [0058]-[0060], and [0064]. Sharp discloses referring to a database comprising data on correlating the gene expression and an effect/disease and evaluating the effect based on the measured gene expression and the correlation ([0002], [0046], and [0071]-[0074]). Sharp discloses the assessment of a plurality of induced genes comprising cytokines, chemokines, immune-related molecules, receptors,

signaling molecules, growth factors, etc. (claim 12, [0054]-[0056]). Sharp discloses that "blood cells" comprise leukocytes [0041]. Sharp discloses that gene expression profiles change in response to "an injury," *e.g.*, inflammatory, autoimmune, and infectious diseases, Alzheimer's disease, *etc.*, which are caused by different factors (*e.g.*, hypoglycemia is caused by injection of hypoglycemics, hypoxia is caused by anesthesia) ([0049]-[0052], [0077]).

Although Sharp discloses a plurality of gene expressions which are altered by different factors (*e.g.*, treatment of a disease), Sharp does not specifically disclose interferon induced and interferon regulated protein genes. Although Sharp discloses changing the gene expression in response to a treatment or other factors, Sharp does not specifically disclose an interferon β treatment.

Veer discloses cloning and sequencing of IFIT4 expression which is regulated by interferon β (p. 274, right col.). Veer discloses mRNA expression in a sample in response to a treatment with IFN- β (p. 274). Veer discloses hybridizing IFIT4 encoding RNA and DNA with specific primers (p. 268).

Veer does not disclose interferon regulation factor genes.

Satoh discloses treatment of a subject with IFN- β, labeling an mRNA sample derived from the treated subject, hybridizing mRNA with primers specific for IRF-7 encoding gene, and detecting fluorescence indicative of a gene expression level (p.682-683). Satoh discloses simultaneous assessing the level of expression of differing genes, *e.g.*, genes encoding MHC class I HLA-C, IRF-7, ICAM-1, pleiotropnin, IRF-1, and STAT1 (p. 683).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method Sharp to evaluate an interferon β treatment and detect the gene

expression of IFIT4 and IRF-7 encoding genes, such as taught by Veer and Satoh, where the motivation would have been to assess effect of an interferon β treatment in Multiple Sclerosis patients and the large range of cellular responses induced by the interferon β, as taught by Veer (p. 267) and Satoh (p. 681, abstract).

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sharp US 2003/0104393, in view of Veer, *Genomics*, 54:267-277 (1998), in view of Satoh, *Neurology*, 57:681-685 (2001), as applied to claim 1 above, and further in view of Nomiyama, *J. Interferon and Cytokine Res.*, 19(3):227-234 (1999).

Sharp, Veer, and Satoh make obvious the method of claim 1, as set forth above. Veer discloses IFIT4 protein gene. Satoh discloses IRF-7 protein gene.

Although Sharp discloses chemokine protein genes, Sharp, Veer, and Satoh doe not specifically disclose SCYA2 chemokine protein gene.

Nomiyama discloses a plurality of members of chemokine family comprising SCYA1, SCYA2, and SCYA9.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method Sharp, Veer, and Satoh to evaluate an interferon β treatment based on gene expression of SCYA2 encoding gene, such as taught by Nomiyama, where the motivation would have been to assess plurality of effects caused by stimulants, as taught by Nomiyama (abstract).

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sharp US 2003/0104393, in view of Veer, *Genomics*, 54:267-277 (1998), in view of Satoh, *Neurology*, 57:681-685 (2001), in view of Nomiyama, *J. Interferon and Cytokine Res.*, 19(3):227-234 (1999), as applied to claims 1-2 above, and further in view of Seeger, *Blood*, 96(11, Part 2):167b (16 Nov., 2000), and in view of Geng, *Genes*, Chromosomes & Cancer, 26:70-79 (1999).

Sharp, Veer, Satoh, and Nomiyama make obvious the method of claims 1-2, as set forth above.

Although Sharp discloses interleukins, Sharp, Veer, Satoh, and Nomiyama do not specifically disclose IL-18.

Seeger discloses examining the gene expression of a plurality of cytokines, chemokines, and growth factors (abstract). Specifically, Seeger discloses IL-18 and TGFB.

Although Seeger discloses TGFB, he does not specifically disclose TGFB1.

Geng discloses TGFB isoforms, *i.e.*, TGFB1, TGFB2, and TGFB3 (p. 70).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method Sharp, Veer, Satoh, and Nomiyama to assess expression levels of a plurality of cytokines and chemokines, such as taught by Seeger and Geng, where the motivation would have been to understand the association of different gene expression patterns and clinical prognosis, and the implication of a variety of immunological molecules in multiple biological processes, as taught by Seeger (abstract) and Geng (p. 70).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-5, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph. D. can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marina Miller
Examiner
Art Unit 1631

MM

MARJORIE A. MORAN
PRIMARY EXAMINER
Marjorie A. Moran
3/27/06